

93982-00018

Appln. No.: 10/042,614
Amendment Dated March 16, 2007
Reply to Office Action of November 16, 2006

Amendments to the Claims: This listing of claims will replace all prior versions, and listings, of claims in the application

Listing of Claims:

1. (Cancelled)
2. (Cancelled)
3. (Cancelled)
4. (Cancelled)
5. (Cancelled)
6. (Cancelled)
7. (Cancelled)
8. (Cancelled)
9. (Cancelled)
10. (Cancelled)
11. (Cancelled)
12. (Cancelled)
13. (Cancelled)
14. (Cancelled)
15. (Cancelled)
16. (Cancelled)
17. (Cancelled)
18. (Cancelled)
19. (Cancelled)

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20. (Cancelled)
21. (Cancelled)
22. (Cancelled)
23. (Cancelled)
24. (Cancelled)
25. (Cancelled)
26. (Cancelled)
27. (Cancelled)
28. (Cancelled)
29. (Cancelled)
30. (Cancelled)
31. (Cancelled)
32. (Cancelled)
33. (Currently amended) A method for assessing a compound's ability to specifically inhibit JNK kinase activity in a mammal susceptible to or having a neurological condition, comprising:
 - (a) incubating said compound in the presence of ~~about 0.5 μ g to about 2 μ g of purified JNK and about 1 μ g to about 3 μ g of a JNK substrate~~, under conditions sufficient for kinase activity;
 - (b) determining the presence or amount of a phosphorylated JNK substrate, wherein a change in the presence or amount of phosphorylated JNK substrate, when compared to incubating isolated JNK with the JNK substrate absent the compound, is indicative of the compound's ability to inhibit the JNK kinase activity;
 - (c) contacting the compound having an ability to inhibit JNK activity with neuronal cells transfected with a mutated protein or treated with a neurotoxin to induce apoptosis, wherein

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the mutated protein comprises polyglutamine stretch-expanded huntingin or C-terminal 100 amino acids of amyloid precursor protein;

(d) comparing the occurrence of apoptosis in the neuronal cells in the presence of the compound with the occurrence of apoptosis in the neuronal cells in the absence of the compound, wherein the compound having an ability to inhibit the JNK activity has the ability to prevent neuronal cell death when the occurrence of apoptosis in the neuronal cells in the presence of the compound is less than the occurrence of apoptosis in the neuronal cells in the absence of the compound;

(e)(e) administering to an animal said compound under conditions sufficient to allow for proper pharmacodynamic absorption and distribution thereof in the animal;

(f)(e) harvesting a neuronal tissue sample from the animal and

(g)(e) determining apoptosis in the tissue sample;

(h)(f) correlating the results of steps (d)(b) and (g)(e) wherein a decrease in apoptosis in the neuronal tissue sample, when compared to apoptosis in a neuronal tissue sample from an animal not administered the compound, as determined in step (g)(e), and wherein the occurrence of apoptosis in the neuronal cells in the presence of the compound is less than the occurrence of apoptosis in the neuronal cells in the absence of the compound-a decrease in the presence or amount of the phosphorylated JNK substrate, when compared to incubating JNK with the JNK substrate absent the compound, as determined in step (d)(b), taken together, correlate to the compound's ability to specifically inhibit JNK kinase activity in a mammal susceptible to or having a neurological condition.

34. (Original) The method of claim 33, wherein JNK is JNK1, JNK2 or JNK3, or combinations thereof.

35. (Cancelled)

36. (Cancelled)

37. (Cancelled)

38. (Cancelled)

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39. (Cancelled)
40. (Cancelled)
41. (Cancelled)
42. (Cancelled)
43. (Cancelled)
44. (Currently Amended) The method of claim 33, wherein apoptosis in step ~~(g)~~(e) is determined using a TUNEL assay.
45. (Currently Amended) The method of claim 33, wherein apoptosis in step ~~(g)~~(e) is determined by administration of γ -³²P-ATP to the animal and detecting the amount of phosphorylated c-Jun in the neuronal tissue sample.
46. (Currently Amended) The method of claim 33, wherein apoptosis in step ~~(g)~~(e) is determined by Hoechst 33342 staining.
47. (Previously Presented) The method of claim 33, wherein the JNK substrate of step (a) includes c-Jun and a phosphate donor.